Possible Hazards and Toxicological Effects of Tartrazine

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Abstract

Background: An artificial azo dye made from coal tar is tartrazine (E 102). The powder is called synthetic lemon yellow, and it has an orange tint. It adds color to a variety of foods, medications, and cosmetics, and is utilized as an additive all over the globe. Tartrazine can enter the human body through two main routes: the oral and dermal. The former includes ingesting foodstuffs, medications, cosmetics, and pharmaceuticals. You can find tartrazine in many different foods and beverages, including juices, cakes, cereal, soups, jellies, candies, and soft drinks. Synthetic food additives are becoming more prevalent, and their safety and effectiveness have come under more scrutiny in recent years. This is especially true when considering the effects on growing bodies. A synthetic azo dye called tartrazine is among these components. Previous studies on the effects of food additives like tartrazine on human health have focused on many different systems in the body. This research collection aimed to summarize those findings. Researchers looked at how tartrazine affected various organs and systems, including the liver, kidneys, lipid profile, neurological system, hyperactivity, behavior, cancer, reproductive and developmental toxicity, and levels of certain bioelements. They also described the various food additives and products that contained tartrazine. Several of the research that were found focused on the pros and cons of tartrazine. The study concludes with a summary of the possible harmful effects of tartrazine on the liver, kidney function, lipid profiles, behavior, carcinogenicity, and suggestions for further research. In this post, we will go over every single negative effect of tartrazine and how safe it is to use. Customers need professional advice on food safety issues, as far as we can tell. There is mounting evidence that tartrazine is toxic, so staying away from it may be wise.

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Introduction:

Flavor, color, consistency, quality, and cost are just a few areas that have benefited from the usage of additives, which currently number over 2,500 compounds. They originated from industrialization and advancements in food processing and treatment (NRC, 1983). All food additives must pass acute, subacute, and chronic toxicity tests before they may be sold to the general population. The effects of food additives should be studied for a long time after they are introduced to the market, though. Concerning the safety of cumulative effects, intra-organism variation, or chronic exposure, there is very little evidence to back these assertions. Surprisingly little is written regarding the medicinal application of tartrazine, despite the abundance of papers addressing the drug's in vivo and laboratory effects (NRC, 1983).

Although there are pros and cons to using food additives, many people do so on a regular basis. Thanks to food additives, contemporary agriculture can provide a vast array of nutritious, tasty, and risk-free foods all year round. Different types of food additives have different beneficial benefits. Nevertheless, food additives may contain a number of metabolites that have been found to be carcinogenic, such as monosodium glutamate and nitrous compounds. The degree to which a food interferes with absorption, excretion, or metabolism determines its toxicity. Recommendations for human consumption safety limits are further complicated by the interaction of multiple substances. Given the high likelihood of toxicity in chemical compounds, it is prudent to treat all novel chemicals used in nutrition as potentially dangerous until their safety is confirmed. A number of people experience adverse reactions to food additives, including gastrointestinal problems, skin irritation, vomiting, diarrhea, or even a rise in core body temperature. In addition, some food additives deplete vitamins already present in food (for example, adding caramel to a dish makes people less likely to get enough vitamin B6), make subpar food look better, and hide the taste of less appealing ingredients. The nutritional value of the food may also be diminished during this procedure. Some food colors have been outlawed because of the associations they have with cancer and other forms of tissue harm. The fact that the ubiquitous food ingredient tartrazine can cause a broad range of negative reactions in people is well-established. This class includes conditions such as migraines, anxiety, asthma episodes, double vision, eczema, rash, and even thyroid cancer.

An artificial azo dye made from coal tar is tartrazine (E 102). Synthetic lemon yellow is the name given to the orange powder. Mehedi et al. (2009) notes its widespread use as a food additive for coloring various foods, pharmaceuticals, and cosmetics.

Many meals contain tartrazine, though the exact levels can vary from brand to brand and even from chef to chef. Many nowadays choose to use natural dyes such as annatto, malt color, or beta carotene instead, or try to stay away from it completely. Sugary snacks, cotton candy, corn flakes, flavored chips (Doritos and Nachos), cake mixes, soups, jams, sauces, ice cream, some rice, candy, chewing gum, marzipan, jelly, gelatins, mustard, marmalade, yoghurt, noodles, fruit snacks, fruit products, chips, and many quick-prep foods are all common sources of tartrazine.

Tartrazine can be present in a variety of non-food items, including cosmetics, hair care products (including shampoos and conditioners), pastels, crayons, and stamp colors, among others.

The Biological Effects and Metabolism of Tartrazine

A principal metabolite known as sulfanilic acid has been isolated. Tartrazine has been the subject of research about its carcinogenic and mutagenic properties, as well as its ability to trigger allergic reactions including urticaria and asthma due to its metabolic conversion into aromatic amine (sulfanilic acid) by the gut bacteria. (Chequer et al., 2011), probably by mammalian azo reductase in the intestinal wall or liver, following ingestion (Moutinho et al., 2007). Following their full reduction to aromatic amines, the P450 enzyme system oxidizes these azo dyes to N-hydroxy derivatives (Demirkol et al., 2012). Among the many diseases caused by this biotransformation mechanism are anemia, pathological lesions of the brain, liver, kidneys, and spleen, as well as allergic reactions, tumors, and cancer (Chequer et al., 2011). Having said that, tartrazine cannot cause either benign or malignant neoplasias. In addition, at doses of 1225 and 773 mg/kg BW/day, respectively, tartrazine did not have any negative effects on neurobehavior development or reproductive indicators, according to Tanaka (2006). There was no indication of Tartrazine-linked adverse effects on reproduction in previous evaluations. Nevertheless, oxidative stress can be increased through the formation of reactive oxygen species (ROS) such as superoxide anion, hydroxyl radical, and H2O2 during the metabolism of nitrosamines (Bansal et al., 2005).

The impact of tartrazine on sensitivity A wide range of immunologic reactions, including lethargy, anxiety, headaches, clinical depression, purple patches on the skin, and trouble sleeping, have been linked to tartrazine ingestion. A sensitivity to tartrazine can develop after ingestion or skin contact with the substance. Even at modest doses, and for up to 72 hours after exposure, some people report symptoms of tartrazine sensitivity. Some studies have linked it to hyperactivity, thyroid cancer, chromosomal damage, rashes, and asthma attacks in children. Some researchers have linked tartrazine to hyperactivity and obsessive-compulsive disorder in infants. Asthma flare-ups may be precipitated by certain common food additives, such as tartarzine and monosodium glutamate. Many drugs contain tartarzine, which may make asthma worse in some people but not others; on the other hand, MSG can make asthma worse in certain people (Romieu, 2005). Patients with a verified sensitivity to food additives (atopic dermatitis) had an increase in the sulfur-releasing leukotrienes generated by peripheral white blood cells when exposed to tartrazine, according to studies on food additives. According to Worm et al. (2001), these changes could have been caused by a food ingredient that played a role in the pathophysiology of atopic dermatitis.

Several human investigations found that tartrazine ingestion was associated with negative effects such urticaria and vasculitis. While sensitive individuals may react to the level of ADI dose, the EFSA Panel (2009) found that tartrazine appears to be able to cause intolerance responses in few exposed people. Tarrazine was examined in 1984 by the European Commission SCF and in 2016 by JECFA. To determine whether tartrazine really does promote hyperactivity in children, the European Food Safety Authority's Scientific Board on Food Additives and Flavorings conducted an evaluation in 2008 (EFSA, 2008c). The reevaluation of tartrazine (E102) as a food additive was approved by the EFSA ANS Panel in 2009 (EFSA ANS Panel, 2009). In any case, ANVISA, Brazil's Sanitary Surveillance Agency, recently held a consultation regarding the possibility of issuing a ticket alerting atopic patients who consume tartrazine-containing foods and medications of an increase in urticaria, asthma, and allergic rhinitis. In contrast, Pestana et al. (2010) found no statistically significant changes between the groups and no significant respiratory, cutaneous, or cardiovascular responses to 35 mg of tartrazine dye compared to the placebo in a group of atopic subjects with asthma, nasal allergy, pseudo-allergic reactions, or urticaria responses to non-steroidal anti-inflammatory (NSAID) medications.

Impact of Azo dyes on Hepatotoxicity and Liver Enzymes in Food

Prior research up to 2015 found that rats given food colorants, especially at high dosages, had raised hepatic serum enzyme activity (AST and ALT), which may indicate increased permeability, damage, or impairment of the hepatic cells.

The damage to the hepatic cellular and mitochondrial membranes in rats given dietary azo dyes was shown by the activities of AST (mostly found in organelles like mitochondria) and cytoplasm (Senthil et al., 2003). The enzymatic activities of ALT, AST, and ALP were shown to be significantly higher in rats that consumed a high dose of tartrazine (500 mg/kg BW) for 30 days or carmoisine (100 mg/kg BW) compared to the control group. In contrast to the control rats, animals given low doses of tartrazine (15 mg/kg BW) and carmoisine (8 mg/kg BW) showed a substantial increase in alkaline phosphatase and ALT activity, respectively (Amin et al., 2010). Furthermore, tartrazine and other food colors cause liver damage in Swiss albino rats, according to research by Saxena and Sharma (2015). Hepatic MDA, albumin, ALP, and serum total protein levels were all significantly elevated, while SOD, GSH, and CAT levels were significantly decreased. Hepatocyte necrosis, infiltration, vacuolation, and a dramatic shift in the antioxidant defense system are all features of the liver change.

The results of Amin et al. (2010) are in line with those of Mekkawy et al. (1998), who found that two different artificial dyes—ponceau, carmoisine, erythrosine, sunset yellow, tartrazine, fast green, indigotine, brilliant blue, and brilliant black—contain both carmoisine and tartrazine. The researchers attributed the changes in serum ALT, AST, and alkaline phosphatase activities to hepatocellular injury caused by the toxic properties of these dyes, which is characterized by swelling, pyknosis, vacuolation, and necrosis of the hepatic cells. It was hypothesized that synthetic dyes are connected with the tissue impairment of maimly liver, heart, and kidney based on the higher activities of aminotransferases and histological alterations.

One possible explanation for the dramatic increases in aminotransferases is that the hepatic lobules are in a biochemical or pathological state where they are unable to carry out essential duties, which in turn causes an imbalance or disruption in intermediate metabolism. Serum enzyme activities—including ALT, AST, LDH, and ALP—determine the kind and extent of damage because these enzymes leak out of cells.

Groups treated with 10 mg/kg BW of tartrazine demonstrated severe hepatic alterations, enlarged hepatocytes, a single large vacuole spanning the entire cytoplasm, and broad trabeculae from degenerated hepatic cells that compressed and narrowed the sinusoids lumen. Additionally, there was brown pigment deposition inside the Küpffer cells and hepatic fatty degeneration when treated with 7.5 and 10 mg/kg BW of tartrazine, according to histopathological examination. Hemorrhage sites, clogged arteries, and an increase in average liver weight were also not proven (Himri et al., 2011).

According to Meyer et al. (2017), when tartrazine was first administered systemically to mice, it caused a modest periportal fibrosis, increased serum alkaline phosphatase activity, and the migration of inflammatory cells to the area around the portal. In addition, NF- κB activities in the colon and liver were increased by tartrazine alone, without the presence of fibrosis or periportal recruitment of inflammatory cells. In hepatic S9 extracts from mice, tartrazine and its sulphonated metabolites as well as the contaminant blocked sulphotransferase activity. Tartrazine may decrease bile acid sulphation and excretion when administered systemically, rather than oestrogen receptor-mediated transcriptional action.

Tartrazine and its impact on renal function

The renal function tests of urea and creatinine level increased significantly when low or high doses of tartrazine were taken daily for 30 days compared to the control group. The high dose showed a higher significance in serum creatinine level (Amin et al., 2010). These findings are consistent with those of Helal et al. (2000), who investigated the effects of both natural and manufactured food dyes. Furthermore, these findings are consistent with those documented by Ashour and Abdelaziz (2009) for the organic azo dye fast green during a 35-day period. A dose-dependent increase in serum creatinine level was also seen with tartrazine (Himri et al., 2011).

Renal impairment is strongly correlated with elevated urea and creatinine levels (Varely, 1987).

All types of renal disorders, including cystic hydronephrosis, kidney renal tuberculosis, and hypervitaminosis D, a condition characterized by calcium deposition, can lead to renal damage. Renal disease is more reliably predicted by increases in plasma creatinine than by increases in other nitrogenous compounds. In terms of renal histopathology, Himri et al. (2011) found that groups treated with 5, 7.5, and 10 mg/kg BW of Tartrazine exhibited tubular dilatation with thickened basement membrane, tubular degeneration, enlarged glomerular capillaries, intercapillary sclerosis, and glomerulus atrophy, respectively.

Hepatic impairment, swelling, congestion, and kidney apoptosis were experienced by both the kidneys and the liver, along with atrophy of the renal corpuscles. The concentration of the dyes provided had a direct correlation with the degree and severity of the histopathological features that were detected (Rus et al., 2009).

Possible Positive Effects of tartrazine

Researchers found that rats given varying doses of carmoisine and tartrazine, as well as a high dose of tartrazine, had significantly lower hepatic GSH levels and catalase activity (Amin et al., 2010). Hepatic superoxide dismutase (SOD) levels fell dramatically at both the high and low tartrazine dosages, although hepatic malondialdehyde (MDA) levels, a biomarker for oxidative stress, rose sharply at the high dose. Hepatocyte autooxidation and lipid peroxidation, brought on by an increase in free radicals or reactive oxygen species (ROS), can lead to clear hepatic damage and the secretion of the enzymes ALT and AST, which are involved in liver function.

Researchers are of the firm belief that the use of these potentially harmful colors in food should be reevaluated because tartrazine may cause oxidative impairment through the reduction of glutathione (GSH), the cell's primary antioxidant, and a notable rise in malondialdehyde (MDA) levels (Demirkol et al., 2012). Researchers found that compared to other groups of male rat pups, those exposed to the synthetic azo dye tartrazine had significantly higher concentrations of malondialdehyde (MDA) in their brain cortex and significantly lower levels of antioxidant biomarkers (SOD, catalase, and GSH) (Mohamed et al., 2015; Saxena and Sharma, 2015). It is proposed that regular beverage consumption may increase the risk of pathophysiology linked to reactive oxygen species (ROS) and peroxyl radical-facilitated events. Thus, real food is the only kind that can be considered healthy; foods of excellent quality do not require additives like Tartrazine or artificial colors to be nutritious.

Effect of tartrazine on the nervous system, hyperactivity and behavior

In a 30-day animal study, tartrazine at doses ranging from 125 to 500 mg/kg had an adverse effect on learning and memory. This may be due to the fact that tartrazine promotes lipid peroxidation metabolites and reactive oxygen species (ROS), inhibits endogenous enzymes that protect brain tissue from damage, and so on (Gao et al., 2011). It appears that the ADI rate of daily tartrazine consumption is reasonably innocuous, based on the available evidence; nevertheless, it is highly improbable that exposure will occur after food consumption. Various animal models, including the elevated plus-maze, open ground, and dark-light transition trials, demonstrated that male Wistar rats exposed to 0, 1, and 2.5% dosages of tartrazine in their drinking water exhibited hyperactivity, antisocial behavior, and anxiety (Kamel & El-lethey, 2011). Additionally, tartrazine at dosages of0.05,0.15, and 0.45% had some antagonistic effects on neurobehavioral indicators throughout generations of mice, according to Tanaka et al. (2008). Tartrazine changed neurobehavioral characteristics in nursing mice depending on the dose (Tanaka, 2006). A clinical study examined the effects of a combination of carmoisine, tartrazine, and sunset yellow on the behavior of children aged 3 to 9. The results showed that children's hyperactive behaviors, including overactivity, inattentiveness, and impulsivity, were exacerbated by the presence of synthetic colors in their diets up until the middle infantile stage. When a child's hyperactivity levels are high, they may also start having trouble in the classroom, especially with reading (McGee et al., 2002). According to McCann et al. (2007), these findings demonstrate that harmful characteristics are present in both extremely hyperactive children and the general population with varying degrees of hyperactivity.

More recently, researchers tested tartrazine for its possible neurotoxic effects; they found that it significantly reduced levels of the brain neurotransmitters gamma amino butyric acid, dopamine, and serotonin, and that immunohistochemical staining with the anti-ssDNA antibody revealed a high number of apoptotic cells in the brain cortex compared to other groups (Mohamed et al., 2015). Based on the research conducted by Basu and Kumar (2017), it was shown that tartrazine had a significant inhibitory influence in fibrillogenesis and demonstrated that food colorants may have anti-amyloidogenic properties.

The DNA-altering and carcinogenic effects of tartrazine

Tartrazine was found to be non-cytotoxic when tested with a range of concentrations from 0.25 to 64.0 mM. But this dye was significantly genotoxic at all concentrations tested. Some injuries remained longer than the +ve control group even after 24 hours of healing, albeit the majority of injuries were responsive. According to Soares et al. (2015), tartrazine has the potential to cause carcinogenesis when consumed for an extended period of time. Spectroscopic titration studies on tartrazine's DNA interaction revealed that the dyes connect to calf thymus DNA and various isosbestic sites, suggesting that the colors bind to the DNA. It appears that tartrazine, used as a food colorant, binds directly to DNA and may have a harmful effect on human cells in vitro (Mpountoukas et al., 2010). One of the first studies to define tartrazine's interaction with an endogenous molecule, bovine hemoglobin, was conducted by Li et al. (2014). Doses more than 10 mg/kg b.w. caused significant DNA damage in the colon and glandular stomach, as shown by

Sasaki et al. (2002). This outcome could be the result of acute dye cytotoxicity or inadequate DNA repair over the three-hour sampling period. The nonmutagenicity of tartrazine was confirmed by Poul et al. (2009), who found that the dye did not increase the amount of micronucleated colonic cells at any of the tested doses compared to the control groups when administered orally up to doses of 2000 mg/kg b.w. Tartrazine causes DNA to become hypochromic without causing any bathochromic effects, according to the spectroscopic and calorimetric investigation. The heat stability of DNA was enhanced by 7.53 K under saturation conditions by tartrazine, albeit (Basu and Kumar, 2016b).

Exploring Tartrazine's Impact on Reproduction and Development

The teratogenic toxic effects of tartrazine were not significantly felt in pregnant Osborne-Mendel rats when administered doses of 0, 60, 100, 400, and 600 mg/kg BW during the first nineteen days of pregnancy (Collins et al., 1990, 1992). In the meanwhile, a study conducted by Mehedi et al. (2009) found that mice exposed to tartrazine at dosages of 0, 0.1, 1.0, and 2.5% for 13 weeks saw a decline in reproductive performance, a drop in sperm count, and an increase in the rate of sperm abnormalities. Because of their potential commonplace consumption, specific clinical trials have evaluated the effects of different colorant mixes (McCann et al., 2007). A definitive conclusion cannot be drawn from these efforts due to their numerous limitations (Amchova et al., 2015). The chemistry and anticipated mechanism of action of a food additive component can inform the choice of a definitive method for evaluating the compound. Also, as there is insufficient evidence and conflicting data to definitively categorize numerous commonly used substances as safe or carcinogenic, ongoing assessment of both new and old chemicals is necessary.

How tartrazine affects the bioelement composition of certain tissues

Researchers have found that rats exposed to tartrazine had significantly altered bioelement levels in their liver, kidneys, and brains, according to a few of papers on the topic (Cemek et al., 2014). One notable change is the elevation of Cu and iron levels in renal tissue. This is significant because Wilson's disease and hepatic cirrhosis are caused by copper accumulation in the tissues (Shazia et al., 2012). It is possible that this effect is caused by the binding of copper and iron to artificial food colorants, which then causes their accumulation in the tissues (Stevens et al., 2013). Taking either a high or low dose of tartrazine had a negative effect on the brain's levels of the trace elements barium and aluminum. Furthermore, tartrazine has been found to have a negative impact on the zinc content of both the liver and the kidneys. This could be because the ROS produced during tartrazine administration peroxide unsaturated fatty acids in cell membranes, reducing their flexibility and disrupting cell function and integrity. As a result, the pumping and selection of activities of the membranes are affected, and the levels of bioelements in tissues may be altered (Cemek et al., 2014).

What happens when tartrazine is added to food and how safe it is

For the purpose of formally defining and evaluating tartrazine's role, several subchronic and chronic feeding research in rats and mice for durations exceeding one year have been conducted (EFSA ANS Panel, 2009). Doses exceeding the ADI of tartrazine—10 g/kg of feed and above—had no discernible effect on the pigmentation of fur, feces, or urine (Borzelleca and Hallagan, 1988). The authors concluded that tartrazine's inadequate metabolism was proven by its presence in children's diet and the existence of discolouration in bodily fluids. The verification by those in charge of its security is now slightly out of date. However, this evaluation does include a number of papers that were published not long ago. This inaugural study synthesizes the majority of the existing literature on tartrazine, its effects on hyperactivity, behavior, carcinogenicity, reproductive and developmental toxicity, and oxidative stress biomarkers, as well as on certain bioelement levels. On top of that, it gives some crucial advice on food additives that people should follow for their own health. Nevertheless, there is a need for further evidence about tartrazine and health in various aspects.

Summary and Suggestions

Tartrazine has multiple negative impacts on different bodily systems and organs, as shown in the available literature and gathered evidence. To begin, it is clear that even at low levels, food additives like tartrazine, a colorant, have a negative impact on and alter biochemical indicators in vital organs like the liver and kidneys. Due to the hepatic oxidative stress induced by the creation of ROS, the risk increases with increasing dosages and daily consumption for 30 days. The harmful effects of tartrazine can be experienced by children due to their frequent consumption of these compounds in a variety of items, including chocolates, gum, chips, drinks, and many more. Also, the good bacteria in your gut can turn tartrazine into aromatic amines, which they can then transform into nitrosamine. Reactive Oxygen Species are released here. Educating the public on the potential dangers of these food azo dyes is, hence, crucial. As a third point, children's growth and weight can be impacted by these food additives because they limit their usual food consumption. Also, hypersensitivity and allergic reactions can be triggered by the azo dye group, which includes tartrazine. It is important to minimize tartrazine consumption, especially in youngsters, as it is a food ingredient. The fourth point is that all current findings, including data from studies on the neurological system, behavior, organ injuries, and results concerning issues of genotoxicity, reproductive toxicity, and chronic carcinogenicity/toxicity, should be made available, and that safety evaluations of tartrazine's effect on health should be updated continuously using modern methodological approaches. Lastly, the type and amount of food additives added to many goods have never been disclosed by the corporations who make them. The general population has no way of knowing what kinds of food additives they have eaten or how much of them. In light of this, it is imperative that food manufacturers provide the names and amounts of food additives in their products, especially those marketed to children. Additionally, manufacturers should pay closer attention to labeling in order to provide clear and detailed information, which is especially important for people who have food allergies. At last, the available evidence shows that tartrazine is not only worthless as a nutritional addition but also has the potential to have adverse effects. Avoiding consuming it is highly advised.

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